

09/980864

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JC10 Rec'd PCT/PTO 07 DEC 2001

PATENT

Attorney Docket No. 02508.0095

CUSTOMER NUMBER 22,852

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re U.S. national phase of )  
PCT/IB01/00544 )  
Inventor: Renato PEDRAZZI ) Group Art Unit:  
Serial No.: Not Yet Assigned ) Examiner:  
Filed: December 7, 2001 )  
For: DEVICE AND METHOD FOR )  
CONTROLLING INFUSION OF A )  
LIQUID IN AN )  
EXTRACORPOREAL BLOOD )  
CIRCUIT )

**Assistant Commissioner for Patents  
Washington, DC 20231**

**BOX: PCT**

Sir:

**PRELIMINARY AMENDMENT**

Prior to examination, please amend the above-identified application as follows:

**IN THE SPECIFICATION**

Please amend the specification as follows:

Page 1, after the title, insert the following new paragraph, section headings, and subheading as follows:

**--CROSS REFERENCE TO RELATED APPLICATIONS**

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This application is a national phase application based on PCT/IB01/00544, filed April 2, 2001, and claims the priority of Italian patent application no, TO2000A000333, filed April 7, 2000.

BACKGROUND OF THE INVENTION

Field of the Invention --.

Page 1, before line 5, add the following new subheading:

--DESCRIPTION OF THE RELATED ART--

Page 3, before line 4, add the following new section heading:

--SUMMARY OF THE INVENTION--.

Page 6, before line 23, add the following new section heading:

--BRIEF DESCRIPTION OF THE DRAWINGS--

Page 7, before line 5, add the following new section heading:

--DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT--

IN THE CLAIMS:

Please cancel now pending claims 1-21 without prejudice or disclaimer and substitute new claims 22-47 therefor as follows:

22. (New) A dialysis machine comprising:

a filter having a blood compartment and a dialysis liquid compartment separated by a semi-permeable membrane;

an extracorporeal blood circuit having an arterial pipe connected to an inlet of the blood compartment and a venous pipe connected to an outlet of the blood compartment;

a dialysis liquid circuit having a supply pipe connected to an inlet of the dialysis liquid compartment and a drain pipe connected to an outlet of the dialysis liquid compartment;

an infusion circuit having a pre-dilution pipe connected to the arterial pipe and a post-dilution pipe connected to the venous pipe;

means for varying the flow of an infusion liquid in the pre-dilution pipe and in the post-dilution pipe , and

control means for controlling the flow varying means so that the flow of the infusion liquid in the pre-dilution pipe and the post-dilution pipe matches a determined sequence.

23. (New) The dialysis machine according to claim 22, wherein the control means comprises means for determining the infusion sequence from at least one characteristic value ( $FF$ ,  $TMP_{ave}$ ,  $K_{uf}$ ) correlated with concentration of the blood ( $CE$ ) and/or filtration efficiency of the filter.

24. (New) The dialysis machine according to claim 23, wherein the control means comprises means for comparing the characteristic value ( $FF$ ,  $TMP_{ave}$ ,  $K_{uf}$ ) with a series of intervals ( $I1...x$ ,  $IT1...x$ ,  $IK1...x$ ), each interval ( $I1...x$ ,  $IT1...x$ ,  $IK1...x$ ) being associated with at least a predetermined control signal ( $S$ ,  $G$ ,  $H$ ,  $L$ ).

25. (New) The dialysis machine according to claim 24, wherein the infusion varying means comprises a valve means for alternately occluding the pre-dilution pipe and the post-dilution pipe, and in that the predetermined control signal ( $G$ ) defines a sequence for opening and closing the valve means.

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26. (New) The dialysis machine according to claim 24, wherein the infusion varying means comprises an infusion pump for circulating the infusion liquid, and in that the predetermined control signal (L) is for regulating the flow rate (IR) of liquid generated by the infusion pump.

27. (New) The dialysis machine according to claim 24, further comprising an ultrafiltration pump for causing ultrafiltration of plasma water through the membrane of the filter, and wherein the predetermined control signal (S) is for regulating the flow rate (UFR) of liquid generated by the ultrafiltration pump.

28. (New) A dialysis machine according to claim 24, further comprising a bubble trap connected to the arterial pipe and a bubble trap connected to the venous pipe and means for injecting or withdrawing air into/from the bubble traps so as to adjust the level of liquid therein, and wherein the predetermined control signal (S) is for controlling the means for injecting or withdrawing air into/from the bubble traps.

29. (New) A dialysis machine according to claim 23, further comprising:  
means for determining an ultrafiltration flow rate (UFR) of plasma water through the membrane of the filter;

means for determining the haematocrit (Hct) at the inlet of the filter, and

means for calculating the characteristic value as a filtration factor (FF) equal to  $UFR/[Q_b(1-Hct)]$ .

30. (New) A dialysis machine according to claim 29, wherein the means for determining the haematocrit (Hct) comprises means for determining the haemoglobin concentration at the inlet of the filter and means for dividing the haemoglobin concentration by a constant coefficient.

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31. (New) A dialysis machine according to claim 23, further comprising:

means for measuring the blood pressure values ( $P_{bo}$ ,  $P_{bi}$ ) at the inlet and at the outlet of the blood compartment of the filter;

means for measuring the dialysis liquid pressure values ( $P_{di}$ ,  $P_{do}$ ) at the inlet and at the outlet of the dialysis liquid compartment of the filter;

means for calculating an inlet transmembrane pressure value ( $TMP_i$ ) as the difference between the pressure value ( $P_{bi}$ ) at the inlet of the blood compartment and the pressure value ( $P_{do}$ ) at the outlet of the dialysis liquid compartment and an outlet transmembrane pressure value ( $TMP_o$ ) as the difference between the pressure value ( $P_{bo}$ ) at the outlet of the blood compartment and the pressure value ( $P_{di}$ ) at the inlet of the dialysis liquid compartment; and

means for calculating the characteristic value as a mean transmembrane pressure value ( $TMP_{ave}$ ) equal to  $[TMP_i - TMP_o]/2$ .

32. (New) A dialysis machine according to claim 31, further comprising:

means for determining an ultrafiltration flow rate (UFR) of plasma water through the membrane of the filter; and

means for calculating the characteristic value as an actual permeability ( $K_{uf}$ ) equal to the ratio between the ultrafiltration flow rate (UFR) and the mean transmembrane pressure value ( $TMP_{ave}$ ).

33. (New) A dialysis machine comprising:

a filter having a blood compartment and a dialysis liquid compartment separated by a semi-permeable membrane;

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an extracorporeal blood circuit having an arterial pipe connected to an inlet of the blood compartment and a venous pipe connected to an outlet of the blood compartment;

a dialysis liquid circuit having a supply pipe connected to an inlet of the dialysis liquid compartment and a drain pipe connected to an outlet of the dialysis liquid compartment;

an infusion circuit having a main pipe which forks into a pre-dilution pipe connected to the arterial pipe and a post-dilution pipe connected to the venous pipe;

a valve set arranged downstream from the fork on the pre-dilution and post-dilution pipes;

an infusion pump on the main pipe supplying a flow IR; and

a control unit operating the infusion pump, for causing a variation of the infusion flow rate, and acting upon the valve set, for causing a particular distribution of the flow of the infusion liquid in the pre-dilution pipe and the post-dilution pipe, the flow of the infusion liquid in the pre-dilution pipe and the post-dilution pipe being caused to match a determined infusion sequence determined from at least one characteristic value (FF,  $TMP_{ave}$ ,  $K_{uf}$ ) correlated with a concentration of the blood ( $C_E$ ) and/or a filtration efficiency of the filter.

34. (New) A dialysis machine comprising:

a filter having a blood compartment and a dialysis liquid compartment separated by a semi-permeable membrane;

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an extracorporeal blood circuit having an arterial pipe connected to an inlet of the blood compartment and a venous pipe connected to an outlet of the blood compartment;

a dialysis liquid circuit having a supply pipe connected to an inlet of the dialysis liquid compartment and a drain pipe connected to an outlet of the dialysis liquid compartment;

an infusion circuit having a main pipe which forks into a pre-dilution pipe connected to the arterial pipe and a post-dilution pipe connected to the venous pipe;

a valve set arranged downstream from the fork on the pre-dilution and post-dilution pipes;

an infusion pump on the main pipe supplying a flow IR;

a bubble trap connected to the arterial pipe and a bubble trap connected to the venous pipe;

a compressed air line comprising a main pipe which forks into two secondary pipes and , respectively connected to the arterial and venous bubble traps;

a valve set arranged at the connection between the main and secondary air pipes; and

a control unit

determining at least one characteristic value ( $FF$ ,  $TMP_{ave}$ ,  $K_{uf}$ ) correlated with a concentration of the blood ( $C_E$ ) and/or a filtration efficiency of the filter,

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comparing the characteristic value ( $FF$ ,  $TMP_{ave}$ ,  $K_{uf}$ ) with a series of intervals ( $I1...x$ ,  $IT1...x$ ,  $IK1...x$ ), each interval ( $I1...x$ ,  $IT1...x$ ,  $IK1...x$ ) being associated with corresponding values of respective control signals ( $S$ ,  $G$ ,  $H$ ,  $L$ ),  
ascribing defined values to the corresponding output signals ( $G$ ,  $H$ ,  $S$  and  $L$ ) for operating, respectively, the valve sets, the ultrafiltration pump, and the infusion pump,  
operating the infusion pump with output signal( $L$ ), for causing a variation of the infusion flow rate,  
acting upon the valve set with output signal( $G$ ), for causing a particular distribution of the flow of the infusion liquid in the pre-dilution pipe and the post-dilution pipe,  
acting on pump with output signal( $S$ ), for causing a variation of ultrafiltration flow rate  $UFR$ , and  
adjusting the valve set with output signal ( $H$ ) to change an amount of air inside the bubble traps.

35. (New) A dialysis machine according to claim 34, comprising:

a haemoconcentration sensor at the inlet of the filter for producing a haemoconcentration signal  $CE$ , the control unit calculating haematocrit ( $Hct$ ) at the inlet of the filter and the characteristic value as a filtration factor ( $FF$ ) equal to  $UFR/[Q_b(1-Hct)]$ , where( $UFR$ )is a set ultrafiltration flow rate of plasma water through the membrane of the filter.

36. (New) A dialysis machine according to one of the claim 34, comprising:



sensors for measuring the blood pressure values ( $P_{bo}$ ,  $P_{bi}$ ) at the inlet and at the outlet of the blood compartment of the filter; and

sensors for measuring the dialysis liquid pressure values ( $P_{di}$ ,  $P_{do}$ ) at the inlet and at the outlet of the dialysis liquid compartment of the filter;

the control unit calculating an inlet transmembrane pressure value ( $TMP_i$ ) as the difference between the pressure value ( $P_{bi}$ ) at the inlet of the blood compartment and the pressure value ( $P_{do}$ ) at the outlet of the dialysis liquid compartment and an outlet transmembrane pressure value ( $TMP_o$ ) as the difference between the pressure value ( $P_{bo}$ ) at the outlet of the blood compartment and the pressure value ( $P_{di}$ ) at the inlet of the dialysis liquid compartment; and

the control unit calculating the characteristic value as a mean transmembrane pressure value ( $TMP_{ave}$ ) equal to  $[TMP_i - TMP_o]/2$ .

37. (New) A dialysis machine according to claim 34, wherein the control unit calculates the characteristic value as an actual permeability ( $K_{uf}$ ) equal to the ratio between the set ultrafiltration flow rate (UFR) and the mean transmembrane pressure value ( $TMP_{ave}$ ).

38. (New) A method for infusing an infusion liquid in an extracorporeal blood circuit of a dialysis liquid machine, the extracorporeal blood circuit having an arterial pipe connected to an inlet of a blood compartment of a filter, and a venous pipe connected to an outlet of the blood compartment, the filter having a blood compartment and a dialysis liquid compartment separated by a semi-permeable membrane,

comprising the steps of:

determining an infusion sequence from at least one characteristic value (FF, TMP<sub>ave</sub>, K<sub>uf</sub>) correlated with the concentration of the blood (CE) and/or a filtration efficiency of the filter, and

infusing the infusion solution in either one or both of the arterial pipe and the venous pipe in accordance with the determined infusion sequence.

39. (New) A method according to claim 38, further comprising the step of comparing the characteristic value (FF, TMP<sub>ave</sub>, K<sub>uf</sub>) with a series of intervals (I<sub>1...x</sub>, IT<sub>1...x</sub>, IK<sub>1...x</sub>), each interval (I<sub>1...x</sub>, IT<sub>1...x</sub>, IK<sub>1...x</sub>) being associated with at least a predetermined control signal (S, G, H, L).

40. (New) A method according to claim 39, wherein the predetermined control signal (G) defines a sequence for opening and closing a valve means arranged for alternately occluding a pre-dilution infusion pipe connected to the arterial line and a post-dilution infusion pipe connected to the venous line.

41. (New) A method according to claim 39, wherein the predetermined control signal (L) is for regulating the flow rate (IR) of liquid generated by an infusion pump for circulating the infusion liquid.

42. (New) A method according to claim 39, wherein the predetermined control signal (S) is for regulating the flow rate (UFR) of liquid generated by a ultrafiltration pump for causing ultrafiltration of plasma water through the membrane of the filter.

43. (New) A method according to claim 39, wherein the predetermined control signal (S) is for controlling means for injecting or withdrawing air into/from bubble traps respectively connected to the arterial pipe and to the venous pipe.

44. (New) A method according to claim 38, further comprising the steps of:

determining a ultrafiltration flow rate (UFR) of plasma water through the membrane of the filter;

determining the haematocrit (Hct) at the inlet of the filter, and

calculating the characteristic value as a filtration factor (FF) equal to  $UFR/[Q_b(1-Hct)]$ .

45. (New) A method according to claim 44, wherein the step of determining the haematocrit (Hct) comprises the step of determining the haemoglobin concentration at the inlet of the filter and the step of dividing the haemoglobin concentration by a constant coefficient.

46. (New) A method according to claim 38, further comprising the steps of:  
measuring the blood pressure values ( $P_{bo}$ ,  $P_{bi}$ ) at the inlet and at the outlet of the blood compartment of the filter;

measuring the dialysis liquid pressure values ( $P_{di}$ ,  $P_{do}$ ) at the inlet and at the outlet of the dialysis liquid compartment of the filter;

calculating an inlet transmembrane pressure value ( $TMP_i$ ) as the difference between the pressure value ( $P_{bi}$ ) at the inlet of the blood compartment and the pressure value ( $P_{do}$ ) at the outlet of the dialysis liquid compartment and an outlet transmembrane pressure value ( $TMP_o$ ) as the difference between the pressure value ( $P_{bo}$ ) at the outlet of the blood compartment and the pressure value ( $P_{di}$ ) at the inlet of the dialysis liquid compartment; and

calculating the characteristic value as a mean transmembrane pressure value ( $TMP_{ave}$ ) equal to  $[TMP_i - TMP_o]/2$ .

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47. (New) A method according to claim 46, further comprising the steps of:  
determining a ultrafiltration flow rate (UFR) of plasma water through the membrane of the filter; and  
calculating the characteristic value as an actual permeability ( $K_{uf}$ ) equal to the ratio between the ultrafiltration flow rate (UFR) and the mean transmembrane pressure value ( $TMP_{ave}$ ).

**IN THE ABSTRACT**

Add new page 24 after the claims, adding the following ABSTRACT OF THE DISCLOSURE. A new separate page 24 is enclosed.

**--ABSTRACT OF THE DISCLOSURE**

A dialysis machine having  
an extracorporeal blood circuit having an arterial pipe and a venous pipe respectively connected to an inlet and an outlet of a blood compartment of a filter having a blood compartment and a dialysis liquid compartment separated by a semi-permeable membrane;  
means for determining a sequence of infusion of a liquid in the extracorporeal blood circuit, from at least one characteristic value ( $FF$ ,  $TMP_{ave}$ ,  $K_{uf}$ ) correlated with the concentration of the blood ( $CE$ ) and/or a filtration efficiency of the filter; and  
means for infusing the infusion solution in the arterial pipe and in the venous pipe in accordance with the determined infusion sequence.

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**ABSTRACT OF THE DISCLOSURE**

A dialysis machine having

an extracorporeal blood circuit having an arterial pipe and a venous pipe respectively connected to an inlet and an outlet of a blood compartment of a filter having a blood compartment and a dialysis liquid compartment separated by a semi-permeable membrane;

means for determining a sequence of infusion of a liquid in the extracorporeal blood circuit, from at least one characteristic value (FF,  $TMP_{ave}$ ,  $K_{uf}$ ) correlated with the concentration of the blood ( $C_E$ ) and/or a filtration efficiency of the filter; and

means for infusing the infusion solution in the arterial pipe and in the venous pipe in accordance with the determined infusion sequence.

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